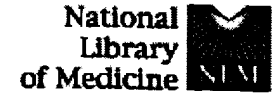

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Search	Most Recent Queries	Time	Result
#46	Search **plasminogen and lethal factor** Limits: **Publication Date to 1998**	17:08:45	16
#45	Search **plasminogen and anthrax** Limits: **Publication Date to 1998**	17:08:32	0
#44	**Related Articles** for **PubMed** (Select **1327517**)	17:07:46	102
#42	Search **target and plasminogen and toxin AND CANCER** Limits: **Publication Date to 1998**	17:06:58	6
#41	Search **plasminogen and toxin AND CANCER** Limits: **Publication Date to 1998**	17:06:46	78
#40	Search **plasminogen and toxin** Limits: **Publication Date to 1998**	17:06:37	560
#38	**Related Articles** for **PubMed** (Select **8226837**)	17:05:36	147
#5	**Related Articles** for **PubMed** (Select **11278833**)	17:04:23	137
#35	Search **tpa AND cancer and expression** Limits: **Publication Date to 1998**	16:46:19	1117
#33	Search **tpa AND BOWES** Limits: **Publication Date to 1998**	16:44:54	15
#27	Search **tpa AND upa AND expression AND cancer** Limits: **Publication Date to 1998**	16:41:19	35
#28	Search **tpa AND upa AND expression AND cancer** Field: **All Fields,** Limits: **Publication Date to 1998, Review**	16:33:19	1
#26	Search **tpa AND upa AND expression** Limits: **Publication Date to 1998**	16:32:57	119
#25	Search **tpa AND upa** Limits: **Publication Date to 1998**	16:32:26	315
#22	**Related Articles** for **PubMed** (Select **9674732**)	16:29:38	815
#20	**Related Articles** for **PubMed** (Select **7947088**)	16:27:34	111
#16	Search **upa AND myelogenous leukemia** Limits: **Publication Date to 1998**	16:26:27	13
#15	Search **upa AND leukemia** Limits: **Publication Date to 1998**	16:25:55	26
#8	**Related Articles** for **PubMed** (Select **7927776**)	15:40:50	134

#11 Search **lethal factor and cancer and plasminogen** Limits: **Publication Date to 1998**	14:21:48	2
#10 Search **lethal factor and cancer** Limits: **Publication Date to 1998**	14:21:31	377
#9 Search **leppla and lethal factor and cancer** Field: **All Fields,** Limits: **Publication Date to 1998**	14:20:14	1
#6 Search **plasminogen and lethal factor**	14:19:38	31
#3 Search **leppla and lethal factor and cancer**	12:53:40	9
#2 Search **leppla and lethal factor**	12:53:27	67
#1 Search **leppla**	12:53:15	152

Clear History

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  FILE 'MEDLINE' ENTERED AT 10:57:42 ON 18 NOV 2004
                E LEPPLA S/AU
L1           116 S LEPPLA S?/AU
L2           433 S LETHAL FACTOR
L3          1325 S PROTECTIVE ANTIGEN
L4           188 S L3 AND L2
L5           188 S L4 AND L2
L6       1671881 S CANCER? OR TUMOR? OR NEOPLAS? OR METASTA?
L7            13 S L5 AND L6
L8         27177 S PLASMINOGEN ACTIVATOR
L9             3 S L8 AND L7
L10          188 S L2 AND L3
L11           13 S L10 AND L6
L12            3 S L8 AND L11

     FILE 'CANCERLIT' ENTERED AT 11:04:32 ON 18 NOV 2004
L13            9 S LEPPLA S?/AU
L14           22 S LETHAL FACTOR
L15           68 S PROTECTIVE ANTIGEN
L16         5939 S PLASMINOGEN ACTIVATOR
L17           54 S ANTHRAX
L18           11 S L17 AND L14
L19         6646 S PLASMINOGEN
L20            1 S L19 AND L18

     FILE 'CAPLUS' ENTERED AT 11:06:04 ON 18 NOV 2004
L21          151 S LEPPLA S?/AU
L22          567 S LETHAL FACTOR
L23         1402 S PROTECTIVE ANTIGEN
L24        25343 S PLASMINOGEN
L25       687350 S CANCER? OR TUMOR? OR NEOPLAS? OR METASTA?
L26            6 S L22 AND L24
L27            5 S L26 AND L25

     FILE 'PCTFULL' ENTERED AT 11:07:26 ON 18 NOV 2004
L28            6 S LEPPLA S?/AU
L29          246 S LETHAL FACTOR
L30         8577 S PLASMINOGEN
L31        82388 S CANCER? OR TUMOR? OR NEOPLAS? OR METASTA?
L32           25 S L29 AND L30
L33           24 S L32 AND L31
L34            2 S L33 NOT PY>1999

     FILE 'MEDLINE, CANCERLIT, CAPLUS, PCTFULL' ENTERED AT 11:09:56 ON 18 NOV
     2004
L35            7 DUP REM L12 L20 L27 L34 (4 DUPLICATES REMOVED)
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L35 ANSWER 7 OF 7 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 1998049311 PCTFULL ED 20020514
TITLE (ENGLISH): RICIN-LIKE TOXIN VARIANTS FOR TREATMENT OF **CANCER**, VIRAL OR PARASITIC INFECTIONS
TITLE (FRENCH): VARIANTES DE TOXINES DE TYPE RICIN DESTINEES AU TRAITEMENT D'INFECTIONS **CANCEREUSES**, VIRALES OU PARASITAIRES
INVENTOR(S): BORGFORD, Thor
PATENT ASSIGNEE(S): DE NOVO ENZYME CORPORATION;
BORGFORD, Thor
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9849311	A2	19981105

DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1998-CA394	A	19980430
PRIORITY INFO.:	US 1997-60/045,148		19970430
	US 1997-60/063,715		19971029

ANSWER 2 OF 3 MEDLINE on STN
ACCESSION NUMBER: 2003031708 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12525700
TITLE: Potent antitumor activity of a urokinase-activated engineered anthrax toxin.
AUTHOR: Liu Shihui; Aaronson Hannah; Mitola David J; Leppla Stephen H; Bugge Thomas H
CORPORATE SOURCE: Oral Infection and Immunity Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD 20892, USA.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2003 Jan 21) 100 (2) 657-62. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20030123
Last Updated on STN: 20030225
Entered Medline: 20030224

ED Entered STN: 20030123
Last Updated on STN: 20030225
Entered Medline: 20030224

AB The acquisition of cell-surface urokinase **plasminogen activator** activity is a hallmark of malignancy. We generated an engineered anthrax toxin that is activated by cell-surface urokinase in vivo and displays limited toxicity to normal tissue but broad and potent **tumoricidal** activity. Native anthrax toxin **protective antigen**, when administered with a chimeric anthrax toxin **lethal factor**, Pseudomonas exotoxin fusion protein, was extremely toxic to mice, causing rapid and fatal organ damage. Replacing the furin activation sequence in anthrax toxin **protective antigen** with an artificial peptide sequence efficiently activated by urokinase greatly attenuated toxicity to mice. In addition, the mutation conferred cell-surface urokinase-dependent toxin activation in vivo, as determined by using a panel of plasminogen, **plasminogen activator**, **plasminogen activator** receptor, and **plasminogen activator** inhibitor-deficient mice. Surprisingly, toxin activation critically depended on both urokinase **plasminogen activator** receptor and plasminogen in vivo, showing that both proteins are essential cofactors for the generation of cell-surface urokinase. The engineered toxin displayed potent **tumor** cell cytotoxicity to a spectrum of transplanted **tumors** of diverse origin and could eradicate established solid **tumors**. This **tumoricidal** activity depended strictly on **tumor** cell-surface plasminogen activation. The data show that a simple change of protease activation specificity converts anthrax toxin from a highly lethal to a potent **tumoricidal** agent.

L9 ANSWER 3 OF 3 MEDLINE on STN
ACCESSION NUMBER: 2001276184 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11278833
TITLE: Targeting of **tumor** cells by cell surface urokinase **plasminogen activator** -dependent anthrax toxin.
AUTHOR: Liu S; Bugge T H; Leppla S H
CORPORATE SOURCE: Oral Infection and Immunity Branch and Oral and Pharyngeal Cancer Branch, NIDCR, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: Journal of biological chemistry, (2001 May 25) 276 (21) 17976-84. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20030105
Entered Medline: 20010705

ED Entered STN: 20010709
Last Updated on STN: 20030105
Entered Medline: 20010705

AB Urokinase **plasminogen activator** receptor (uPAR) binds pro-urokinase **plasminogen activator** (pro-uPA) and thereby localizes it near plasminogen, causing the generation of active uPA and plasmin on the cell surface. uPAR and uPA are overexpressed in a variety of human **tumors** and **tumor** cell lines, and expression of uPAR and uPA is highly correlated to **tumor** invasion and **metastasis**. To exploit these characteristics in the design of **tumor** cell-selective cytotoxins, we constructed mutated anthrax toxin-**protective antigen** (PrAg) proteins in which the furin cleavage site is replaced by sequences cleaved specifically by uPA. These uPA-targeted PrAg proteins were activated selectively on the surface of uPAR-expressing **tumor** cells in the presence of pro-uPA and plasminogen. The activated PrAg proteins caused internalization of a recombinant cytotoxin, FP59, consisting of anthrax toxin **lethal factor** residues 1-254 fused to the ADP-ribosylation domain of Pseudomonas exotoxin A, thereby killing the uPAR-expressing **tumor** cells. The activation and cytotoxicity of these uPA-targeted PrAg proteins were strictly dependent on the integrity of the **tumor** cell surface-associated plasminogen activation system. We also constructed a mutated PrAg protein that selectively killed tissue **plasminogen activator**-expressing cells. These mutated PrAg proteins may be useful as new therapeutic agents for **cancer** treatment.